

Biodosimetry of alpha-particle-induced DNA double-strand breaks in murine bones and soft tissues

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Ionizing radiation causes a variety of DNA damages, of which the DNA double-strand break (DSB) stands out as the most hazardous type. The human body is exposed to different types of ionizing radiation on a daily basis. The most relevant source of natural radiation, comprising approximately 40 percent of a person's annual background radiation, is radon gas [1]. Radon (Rn-222) is a radioactive noble gas, which emits three biologically relevant α -particles during its decay chain. Despite its radioactive properties, radon gas is used for its therapeutic effects in radon therapy caves in Bad Gastein and Bad Kreuznach [2].

As part of the GREWIS project, this study is aimed at the biodosimetric measurement of inhaled radon gas in murine tissues. This project is focused on the detection of α -particle-induced DSB tracks in different murine tissues to elucidate the diffusion patterns of radon gas *in vivo* as well as potential organ-specific accumulations.

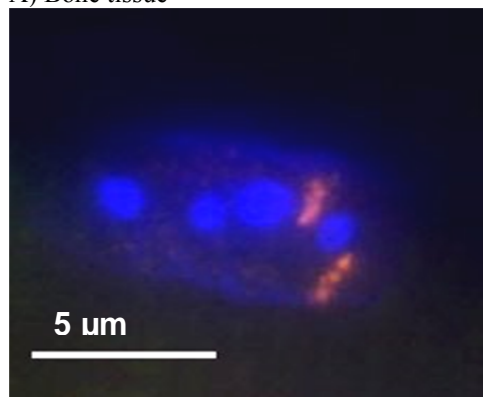
In the past year, three independent *in vivo* radon experiments, using a total of 18 wild type C57BL/6 mice (female, adults) were performed. A radon exposure chamber was used to expose the mice to a specific radon concentration (40 kBq/m³ or 440 kBq/m³) for the duration of one hour. DSBs were visualized in paraffin-embedded tissue sections using highly sensitive immunofluorescence staining for 53BP1 and γ H2AX [3]. Analysis of tissue sections of two radon-exposed mice revealed that 15 minutes after the end of the exposure period (440kBq/m³), excess 53BP1 and γ H2AX foci can be detected in bone (Fig.1A), lung (Fig.1B), heart, kidney, and liver tissues.

As radon therapy is predominantly used for the therapy of chronic inflammatory diseases of the musculoskeletal system, a preferential accumulation of radon decay products in bone tissue was investigated. The current results do not support this hypothesis. Only a slight increase of DSBs, comparable to the level in heart or kidney tissue, was detected in bone samples. Similar levels of DSBs in heart, liver, bone, and kidney tissues support a model in which radon can diffuse freely throughout the body.

Lung tissue sections, on the other hand, showed significantly elevated levels of 53BP1 foci after radon exposure. The accumulation of DSBs in the lung is likely caused by the additional dose that is deposited in this organ due to inhaled radon progeny. As radon decays in the air, radon progeny, with an affinity to adhere to aerosol particles, are formed. These complexes subsequently enter the body through the respiratory tract and accumulate in the bronchioles where radon decay products decay further, hence inducing additional DNA damage. The lung is therefore exposed not only to inhaled radon, but also to radioactive radon decay products.

Future efforts will focus on the comparison of results from radon-exposed mice with foci numbers from mice irradiated with a defined dose of X-rays in order to calculate the dose deposited in specific organs after radon exposure.

A) Bone tissue



B) Lung tissue

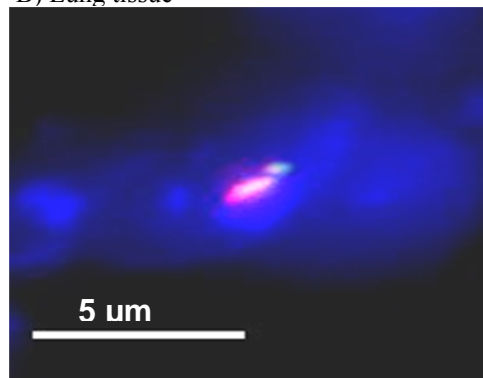


Fig.1: Visualization of DSBs: Tissue samples from mice exposed to 440 kBq/m³ for one hour. Animals were sacrificed 15 minutes after the end of the exposure period. (A) Co-localizing γ H2AX and 53BP1 foci in murine bone tissue. (B) Co-localizing γ H2AX and 53BP1 foci in murine lung tissue.

References

- [1] Bundesamt für Strahlenschutz
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- [3] C. Rübe. Clin Cancer Res (2008) 14:6546-6555

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